

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference BCS 04-5001 PCT	FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/EP2005/002454	International filing date (day/month/year) 04.03.2005	Priority date (day/month/year) 05.03.2004	
International Patent Classification (IPC) or national classification and IPC INV. C12Q1/48 C07K14/415 C12N5/04 C12N15/82 A01H5/00			
Applicant BAYER CROPSCIENCE GMBH et al.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 10 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 21.12.2005		Date of completion of this report 08.05.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized officer Weber, P Telephone No. +31 70 340-	



**INTERNATIONAL PRELIMINARY REPORT
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-104 as originally filed

Sequence listings part of the description, Pages

1-33 as originally filed

Claims, Numbers

1-18 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 5, 9-18

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 5, 9-18

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-4,6-8 .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-4,6-8
	No: Claims	
Inventive step (IS)	Yes: Claims	2-4
	No: Claims	1,6-8
Industrial applicability (IA)	Yes: Claims	1-4,6-8
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)
and /or
2. Non-written disclosures (Rule 70.9)
see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment on
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

Re Item IV

The separate inventions/groups of inventions are:

Invention 1: Claims 1-4,6-8

Methods for identifying proteins (and the corresponding nucleic acid molecules) which exhibit alpha-1,4-glucan phosphorylating enzymatic activity.

Invention 2: Claims 5,9-18 (partially)

Proteins with SEQ ID NOs 2, 4, and 22; nucleic acid molecules with SEQ ID NOs 1, 3, and 21; corresponding genetically modified plant cells; plants containing the genetically modified plant cells.

Invention 3: Claims 5,9-18 (partially)

Protein with SEQ ID NO 10; nucleic acid molecule with SEQ ID NO 9; corresponding genetically modified plant cells; plants containing the genetically modified plant cells.

Invention 4: Claims 5,9-18 (partially)

Protein with SEQ ID NO 16; nucleic acid molecule with SEQ ID NO 15; corresponding genetically modified plant cells; plants containing the genetically modified plant cells.

Invention 5: Claims 5,9-18 (partially)

Protein with SEQ ID NO 26; nucleic acid molecule with SEQ ID NO 25; corresponding genetically modified plant cells; plants containing the genetically modified plant cells.

The technical problem to be solved in the present application is the provision of methods and means for producing plants synthesising a modified starch having elevated phosphate content and/or modified phosphate distribution. The single general concept which can be identified a priori as linking the various claimed inventions and which forms a solution to the above mentioned problem relates to screening for proteins which exhibit alpha-1,4-glucan phosphorylating enzymatic activity. The technical feature of method claims 1 and 2 resides in the extraction of proteins that are specifically bound to phosphorylated alpha-1,4-glucans and the observation of their alpha-1,4-glucan phosphorylating enzymatic activity. Neither the same nor a corresponding special technical feature (Rule 13.2 PCT) is present in any of the proteins of claim 5. No manufacturing relationship exists between the screening methods and these proteins. Further, the screening methods are not methods of using the claimed proteins. There is no single general concept that links the methods to the claimed proteins (Rule 13.1 PCT). Thus, unity of invention is lacking between the methods and the proteins (a priori). While the methods represent one invention (Invention 1, see above) the proteins have to be regarded as representing 4 different inventions (Inventions 2-5, see above) for the following reasons:

The proteins according to claim 5 are defined by a given desired property, namely being "obtainable by a method according to claims 1 to 4". However, the description only provides support and disclosure in the sense of Article 6 and 5 PCT for the proteins having SEQ ID NOs 2,4,10,16,22,26. From these proteins, the proteins having the SEQ ID NOs 2,4,22 have to be regarded as having the same or corresponding technical feature in the sense of Rule 13.2 PCT because they have a common activity, i.e. they all exhibit alpha-1,4-glucan phosphorylating enzymatic activity and require phosphorylated alpha-1,4-glucans as substrate, and share a significant structural element that is essential to the common activity, i.e. a sequence having the SEQ ID NO 5. Consequently, they have to be considered as representing one invention (Invention 2, see above). However, the proteins having the SEQ ID NOs 10,16,26 just share the common enzymatic activity, but do not share a significant structural element that is essential to the activity and hence, there is no disclosure of the same or corresponding technical feature. Consequently, they have to be considered as representing three additional, different inventions (Inventions 3-5, see above).

No fees were paid for Inventions 2-5. Consequently, the examination of the present

application was limited to Invention 1.

Re Item V

1. Reference is made to the following document:

D1: LORBERTH ET AL: "inhibition of a starch-granule-bound protein leads to modified starch and repression of cold sweetening" NATURE BIOTECHNOLOGY, vol. 16, May 1998, pages 473-477, XP002111459

2. NOVELTY (Article 33(2) PCT) - YES

1. The subject-matter of claims 1-4,6-8 **is novel** in the sense of Article 33(2) PCT, because it is not disclosed in the prior art.

3. INVENTIVE STEP (Article 33(3) PCT) - NO

1. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,6-8 **does not involve an inventive step** in the sense of Article 33(3) PCT.

2. Claim 1

D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses (the references in parentheses applying to this document):

A method for identifying a protein which has a binding activity towards phosphorylated alpha-1,4-glucans, wherein a) a protein extract is incubated with phosphorylated alpha-1,4-glucans (paragraph "experimental protocol" on page 476: potato starch granules from potato tubers, which contain an exceptionally high content of covalently bound phosphate were used as phosphorylated alpha-1,4-glucans); b) proteins specifically bound to the phosphorylated

alpha-1,4-glucans from step a) are dissolved; and c) proteins are identified which exhibit a binding activity towards phosphorylated alpha-1,4-glucans used in step b) (paragraph "experimental protocol" on page 476: protein R1 is identified).

From this, the subject-matter of claim 1 differs in that binding to non-phosphorylated alpha-1,4-glucans is studied as well and only those proteins are identified that show an elevated binding activity towards phosphorylated alpha-1,4-glucans compared to non-phosphorylated alpha-1,4-glucans.

The technical effect of this difference relates to the preselection of proteins that might be involved in the phosphorylation of alpha-1,4-glucans.

The problem to be solved by the present invention may therefore be regarded as how to preselect proteins that might be involved in the phosphorylation of alpha-1,4-glucans.

The solution proposed in claim 1 is to study the binding to non-phosphorylated alpha-1,4-glucans as well and to identify just those proteins that show an elevated binding activity towards phosphorylated alpha-1,4-glucans compared to non-phosphorylated alpha-1,4-glucans.

This has to be considered as not involving an inventive step (Article 33(3) PCT) for the following reasons:

Starting from the method disclosed by D1 it is obvious for the person skilled in the art to use the solution proposed in claim 1 in order to solve the problem posed, because a protein that is involved in the phosphorylation of alpha-1,4-glucans necessarily has to interact in some way with the phosphate groups on alpha-1,4-glucans. The general routine method for distinguishing between an interaction of a protein with a modification (i.e. the phosphate groups) and the modified molecule as such (i.e. the alpha-1,4-glucan) is a differential approach using modified molecules (i.e. phosphorylated alpha-1,4-glucans) and unmodified molecules (i.e. unphosphorylated alpha-1,4-glucans). Consequently, the person skilled in the art would arrive at the same solution in order to solve the problem posed without the exercise of inventive

skill.

Consequently, the subject-matter of claim 1 does not involve an inventive step (Article 33(3) PCT).

3. Claims 6,7

The features of claims 6 and 7 merely relate to routine methods for the identification of nucleic acid molecule coding for proteins and do not contribute anything of inventive significance to the claims.

4. Claim 8

Claim 8 relates to a method for identifying a nucleic acid molecule coding for a protein which exhibits alpha-1,4-glucan phosphorylating enzymatic activity. However, it is not conceivable for the person skilled in the art how nucleic acid molecules should be identified according to step c) using antibodies in the absence of additional essential features, because antibodies are believed to be used to identify proteins and not to identify nucleic acids. Consequently, it is assumed that claim 8 in its present state does not work and therefore cannot be inventive in the sense of Article 33(3) PCT.

4. INVENTIVE STEP (Article 33(3) PCT) - YES

1. The subject-matter of claims 2-4 **involves an inventive step** in the sense of Article 33(3) PCT, because the importance of the notion that the proteins to be identified have to require phosphorylated alpha-1,4-glucans as substrates is neither anticipated by the prior art nor obvious to a person skilled in the art, having regard to the prior art.

5. INDUSTRIAL APPLICABILITY (Article 33(4) PCT)

The subject-matter of claims 1-4,6-8 is industrially applicable in the sense of Article 33(4) PCT.